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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/510,531	03/30/2005	Paul Dent	ON/4-32419A	8871

1095 7590 04/15/2010

NOVARTIS
CORPORATE INTELLECTUAL PROPERTY
ONE HEALTH PLAZA 104/3
EAST HANOVER, NJ 07936-1080

EXAMINER	
SZNAIDMAN, MARCOS L	
ART UNIT	PAPER NUMBER
1612	

MAIL DATE	DELIVERY MODE
04/15/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Advisory Action Before the Filing of an Appeal Brief	Application No.	Applicant(s)	
	10/510,531	DENT ET AL.	
	Examiner	Art Unit	
	MARCOS SZNAIDMAN	1612	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 06 April 2010 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:

a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.

b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☒ The Notice of Appeal was filed on *06 April 2010*. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).

4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).

5. ☐ Applicant's reply has overcome the following rejection(s): _____.

6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

7. ☐ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: _____.
   Claim(s) rejected: *17-22*.
   Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).

9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).

10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.

12. ☐ Note the attached Information *Disclosure Statement*(s). (PTO/SB/08) Paper No(s). _____

13. ☐ Other: _____.

/Frederick Krass/
Supervisory Patent Examiner, Art Unit 1612

/MARCOS SZNAIDMAN/
Examiner, Art Unit 1612

Continuation of 11. does NOT place the application in condition for allowance because: Applicant argues that: the instant application does not require any type of specific binding between the CDK inhibitor and the Bcr/Abl kinase in order to the CDK inhibitor to exert its biological function. it is the CDK inhibitor's biological actiovity inhibiting CDK that makes it useful in the present method.
Examiner's response: even if Applicant is correct and the synergistic effect observed with flavopiridol is due only to its interaction with the CDK kinase, Applicant has not provided a representative set of CDK inhibitors for the entire genus claimed. The prior art and the instant application are silent regarding the effect of other CDK inhibitors against leukemia cells resistant to Imatinib, except for the CDK inhibitor flavopiridol. Although all the CDK inhibitors have the common biological effect of inhibiting the CDK kinase, not all of them do it in the same way, and some might have different profiles against different kinases, which are different than the selectivity profile shown by flavopyridol, and as such one can not extrapolate from one single example that most CDK inhibitors will behave like flavopiridol. MPEP 2164.02 states: "Proof of enablement will be required for other members of the claimed genus only where adequate reasons are advanced by the Examiner to establish that a person skilled in the art could not use the genus as whole without ubdue experimentation".
Applicant further argues that: the Examiner has not provided any information which would lead the skilled artisan not to expect some benefit from all the combinations within the scope of the present claims.
Examiner's response: the Examiner again referes to In re Kollman, wherein the court affirmed a rejection of a claim containing the word "synergistic", because the claims were not commensurate in scope with the showing of unexpected results, other than at 1:1 ratio for certain specific combinations. In the instant case, Applicant provided data for only one ratio of flavopiridol and Imatinib (200 nm: 1.5 micromolar).
Applicant argues that: the present claims only embrace those Bcr-Abl positive leukemias wherein the Bcr-Abl is not sufficiently inhibited by Imatinib. The present specification teaches that Imatinib resistance can be overcome by a treatment which combines Imatinib with an agent that provides for CDK inhibition.
Exminer's response: Applicant is claiming: "A method of treating Bcr-Abl-positive leukemia resistant to Imatininb, comprising administering a CDK inhibitor and Imatinib". However, as discussed in previous office action, Applicant has not provided enough data that the above combination will be effective against most of theBcr-Abl mutations, like Thr315Ile which is disproportionately represnted among patients who relapse on these therapies. Since Applicant does not specify against which Bcr-Abl mutations the instant combination is effective, there is no correlation between the data provided by Applicant and the much broader claim: "inhibition of Bcr-Abl-positive leukemia resistant to Imatininb".